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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/306,986	05/07/1999	THUAN QUOC TRINH	0942.4570001	4261

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EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 03/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/306,986

Applicant(s)

TRINH ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8-13,56 and 70-75 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-13,56 and 70-75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicants amendment of claims 8, 9, 70-75 in the paper of 12/11/2003, is acknowledged. Claims 8-13, 56 and 70-75 are at issue and are present for examination.

Applicants' arguments filed on 12/11/2003, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-13, 56 and 70-75 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection was stated in the previous office action. In response to this rejection applicants have amended claims 8, 9 and 70-75 and traverse the rejection as it applies to the newly amended claims.

Applicants submit that the relevant portion of claim 8 has been amended and that thus the claims as presently written are not indefinite and respectfully request reconsideration and withdrawal of this rejection.

Applicants argument is not found persuasive because applicants amendment has not resulted in the addition of an "active RNA degradation step ". As was discussed in the previous office actions as well as the in the previous interview, applicants have not added an active RNA degradation step to the claimed methods. Applicants amendment has merely altered ever so slightly "the conditions under which the mixture is incubated".

As was stated below and previously, the current recited limitation does not necessitate that single-stranded RNA be degraded, but rather it states that merely the mixture be incubated in conditions "under which peptides or polypeptides having ribonuclease activity degrade" single-stranded RNA. As stated previously, the single-stranded RNA need not be degraded, but merely the conditions be such that peptides or polypeptides having ribonuclease activity degrade single stranded RNA. Thus the rejection is maintained for the reasons previously stated.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8, 9, 10, 13 and 71-73 are rejected under 35 U.S.C. 102(b) as being anticipated by Davey et al. (U.S. Patent No: 5,409,818, issued 4/25/1995).

The rejection was stated in the previous office action. In response to this rejection applicants have amended claims 8, 9 and 70-75 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection as the above 112 second paragraph rejection on the basis that applicants amendment has resulted in overcoming the rejection. Applicants further submit that Davey does not disclose conditions under which said peptides or polypeptides having ribonuclease activity degrade single-stranded RNA and therefore, does not anticipate the present invention. Applicants support applicants position on the basis that the ribonuclease used by Davey et al. is "specific for RNA-DNA hybrids" and that Davey et al. states "each enzyme or enzyme preparation should be free of deleterious ribonuclease ("Rnase") activities with the exception of the preferred addition of a ribonuclease activity which is specific for hybrids of RNA and DNA (for example, ribonuclease H)". Applicants thus conclude that Davey et al. does not disclose conditions under which said peptides or polypeptides having ribonuclease activity degrade single-stranded RNA and therefore, does not anticipate the present invention.

Applicants argument continues to be found nonpersuasive for the reasons previously stated. Applicants previous amendment of the claims and applicants continued argument is acknowledged however these are not persuasive in overcoming the current rejection for the reasons discussed above under the 112 second paragraph

rejection. Applicants is reminded that applicants amendment has not resulted in the incorporation of an active RNA degradation step in the claimed method and regardless of what type of RNase Davey et al. teaches, uses, or desires, "the conditions" that Davey et al. teaches are such that "peptides or polypeptides having ribonuclease activity degrade single-stranded RNA".

Thus claims 8, 9, 10, 13 and 71-73, remain anticipated by Davey et al.

Claims 8, 9, 10, 13, and 72 are rejected under 35 U.S.C. 102(e) as being anticipated by Kenten et al. (U.S. Patent No: 6,048,687, filed 6/7/1995).

The rejection was stated in the previous office action. In response to this rejection applicants have amended claims 8, 9 and 70-75 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection on the same basis as the above Davey et al. rejection, on the basis that Kenten et al. teach the same amplification method as that of Davey et al. and thus Kenten et al. does not anticipate the rejected claims for the same reasons discussed above for Davey et al.

Applicants argument is not found persuasive for the same reasons previously stated in this rejection and stated above for the rejection over Davey et al.

Thus claims 8, 9, 10, 13 and 72, remain anticipated by Kenten et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 70, 74 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davey et al. et al. (U.S. Patent No: 5,409,818, issued 4/25/1995).

The rejection was stated in the previous office action. In response to this rejection applicants have amended claims 8, 9 and 70-75 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection as the above rejection based on anticipation by Davey et al. on the basis that Davey et al. does not teach conditions "under which said peptides or polypeptides having ribonuclease activity degrade single-stranded RNA". As discussed above this argument is not found persuasive for the same reasons discussed above. Regardless of what type of RNase Davey et al. teaches, uses, or desires, "the conditions" that Davey et al. teaches are such that "peptides or polypeptides having ribonuclease activity degrade single-stranded RNA". Based on the above there is no need to modify the "conditions" taught by Davey et al., as Davey et al. teach "conditions" under which peptides or polypeptides having ribonuclease activity degrade single-stranded RNA.

Thus claims 70, 74 and 75 remain obvious over Davey et al. et al.

Claims 8-12, 70, 71 and 73 under 35 U.S.C. 103(a) remain rejected as being unpatentable over Major (Biotechniques, Vol 12, No. 1, 1992, pages 40-43) and Maudru et al. (Journal of Virological Methods 66: 247-261, July 1997).

The rejection was stated in the previous office action. In response to this rejection applicants have amended claims 8, 9 and 70-75 and traverse the rejection as it applies to the newly amended claims.

Applicants traversal which follows the same logic as discussed above under the traversal of the 102 rejections based on the conditions of the assay is not found persuasive for the same reasons as discussed above.

Applicants continue to further traverse this rejection on the basis that in contrast to Maudru, Major is concerned with detecting a single point mutation in a plasmid using a simplified allele-specific PCR method and that Major uses a DNA template and DNA oligonucleotides in his assay. Applicants further assert that the small amount of background seen by Major is attributed to the mismatched 3'-nucleotides of the primer and was eliminated by the inclusion of a PCR enhancing reagent, Perfect Match and thus one of skill in the art would have had no motivation to include RNase in the method of Major based on the fact that Major used a DNA template and DNA primers in a PCR assay there is no teaching that RNA has any effect on the assay.

Applicants argument continues to be found nonpersuasive for the following reasons. While it is acknowledged that the specific method taught by Major uses a DNA template and DNA primers, applicant is reminded that Major also teaches similar methods of screening using bacterial lysates which would also involve the presence of

contaminating RNA. Applicants comments referring to a comparison of bacterial lysates and plasmid DNA, referencing "one can get single-base discrimination using unpurified template" and stating that Major attributes the background in the assay to the mismatch of the 3'-nucleotide in the primer to the sequence to be amplified as well as the use of a PCR enhancing compound to reduce spurious bands are acknowledged, however, not found persuasive.

While Major does not attribute background difficulties to contaminating RNA, one of skill in the art would realize that given the employment of the method of Major to bacterial lysates, there would be a substantial amount of background RNA in the preparation. This knowledge in combination with that taught by Maudru et al. stating that the background signal in a similar assay was found to be due to an intrinsic RNA-dependent DNA polymerase activity of the *Taq* DNA polymerase would lead one of skill in the art who was attempting to successfully use a PCR method to screen for small mutations to include a ribonuclease digestion step prior to PCR amplification as a means of making the assay more sensitive. In support of the above, applicants attention is drawn to Major, page 42, middle column, which states "the present results indicate that all three possible terminal T mismatches can be equally discriminated under standard PCR conditions, **especially** when using mini-prep DNA". Such a statement clearly supports that even Major recognized the taught method had different results or sensitivities depending on the template used (noting the reference to "especially"), although Major did not comment on the specific difference of the two

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different types of template preparations. One of skill in the art would understand that the difference was likely the presence of contaminating material, such as RNA.

Thus the rejection of claims 8-12, 70, 71 and 73 is maintained in light of the above and the previous discussion.

Remarks

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

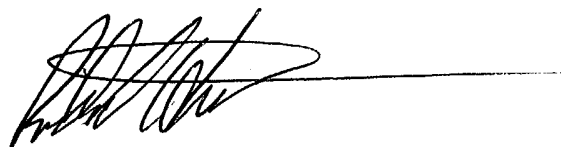
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Richard G. Hutson', followed by a long horizontal line extending to the right.

Richard G Hutson, Ph.D.
Primary Examiner
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rg
3/10/2004